10/658904

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=> d his

     (FILE 'HOME' ENTERED AT 12:20:43 ON 07 APR 2006)

     FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS,
     LIFESCI' ENTERED AT 12:21:52 ON 07 APR 2006
L1             1 S "14171 KINASE?"
L2       1434878 S KINASE?
L3       7629584 S CLON? OR EXPRESS? OR RECOMBINANT
L4            73 S "T-P" MOTIF
L5            49 S L2 AND L4
L6            12 DUP REM L5 (37 DUPLICATES REMOVED)
L7        947418 S (MODULAT? OR ACTIVAT? OR INHIBIT? ) AND L2
L8            42 S "14171"
L9             2 S L7 AND L8
                 E LIBERMANN ROSANNA
                 E LIBERMANN/AU
                 E KAPELLER R/AU
L10          103 S E3
L11            0 S L8 AND L10

=>
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 NEWS  4  DEC 23   New IPC8 SEARCH, DISPLAY, and SELECT fields in USPATFULL/
                   USPAT2
 NEWS  5  JAN 13   IPC 8 searching in IFIPAT, IFIUDB, and IFICDB
 NEWS  6  JAN 13   New IPC 8 SEARCH, DISPLAY, and SELECT enhancements added to
                   INPADOC
 NEWS  7  JAN 17   Pre-1988 INPI data added to MARPAT
 NEWS  8  JAN 17   IPC 8 in the WPI family of databases including WPIFV
 NEWS  9  JAN 30   Saved answer limit increased
 NEWS 10  JAN 31   Monthly current-awareness alert (SDI) frequency
                   added to TULSA
 NEWS 11  FEB 21   STN AnaVist, Version 1.1, lets you share your STN AnaVist
                   visualization results
 NEWS 12  FEB 22   Status of current WO (PCT) information on STN
 NEWS 13  FEB 22   The IPC thesaurus added to additional patent databases on STN
 NEWS 14  FEB 22   Updates in EPFULL; IPC 8 enhancements added
 NEWS 15  FEB 27   New STN AnaVist pricing effective March 1, 2006
 NEWS 16  FEB 28   MEDLINE/LMEDLINE reload improves functionality
 NEWS 17  FEB 28   TOXCENTER reloaded with enhancements
 NEWS 18  FEB 28   REGISTRY/ZREGISTRY enhanced with more experimental spectral
                   property data
 NEWS 19  MAR 01   INSPEC reloaded and enhanced
 NEWS 20  MAR 03   Updates in PATDPA; addition of IPC 8 data without attributes
 NEWS 21  MAR 08   X.25 communication option no longer available after June 2006
 NEWS 22  MAR 22   EMBASE is now updated on a daily basis
 NEWS 23  APR 03   New IPC 8 fields and IPC thesaurus added to PATDPAFULL
 NEWS 24  APR 03   Bibliographic data updates resume; new IPC 8 fields and IPC
                   thesaurus added in PCTFULL
 NEWS 25  APR 04   STN AnaVist $500 visualization usage credit offered

 NEWS EXPRESS  FEBRUARY 15 CURRENT VERSION FOR WINDOWS IS V8.01a,
               CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
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               V8.0 AND V8.01 USERS CAN OBTAIN THE UPGRADE TO V8.01a AT
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FILE 'HOME' ENTERED AT 12:20:43 ON 07 APR 2006

=> file medline embase biosis biotechds scisearch hcaplus ntis lifesci
COST IN U.S. DOLLARS SINCE FILE ENTRY TOTAL SESSION
FULL ESTIMATED COST 0.42 0.42

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FILE 'LIFESCI' ENTERED AT 12:21:52 ON 07 APR 2006
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=> s "14171 kinase/"
<------User Break------>

=> s "14171 kinase?"
L1 1 "14171 KINASE?"

=> d ibib ab

L1 ANSWER 1 OF 1 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
ACCESSION NUMBER: 2004-12766 BIOTECHDS
TITLE: New 14171 protein kinase and nucleic acid, useful for diagnosing or treating diseases with aberrant expression of the 14171 protein kinase, such as cancer, an immunological disorder, inflammation, heart failure and hypertension; recombinant enzyme protein production via plasmid expression in host cell for use in disease therapy
AUTHOR: KAPELLER-LIBERMANN R
PATENT ASSIGNEE: MILLENNIUM PHARM INC
PATENT INFO: US 2004048305 11 Mar 2004
APPLICATION INFO: US 2003-658904 10 Sep 2003
PRIORITY INFO: US 2003-658904 10 Sep 2003; US 2000-182096 11 Feb 2000
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2004-226195 [21]

AB DERWENT ABSTRACT:

NOVELTY - An isolated nucleic acid molecule (I) comprising a fully defined sequence of 3860 or 2355 base pairs (bp) (SEQ ID NO: 1 and 3) as given in the specification; a fragment of a fully defined sequence of 21 bp (SEQ ID NO: 21, 22 or 23) as given in the specification; or encoding a polypeptide having a fully defined sequence of 784 amino acids (SEQ ID NO: 2) as given in the specification, is new.

DETAILED DESCRIPTION - An isolated nucleic acid molecule comprises: (a) a fully defined sequence of 3860 or 2355 bp (SEQ ID NO: 1 and 3) as given in the specification; (b) a fragment of a fully defined sequence of 21 bp (SEQ ID NO: 21, 22 or 23) as given in the specification; (c) a nucleic acid molecule which encodes a polypeptide having a fully defined sequence of 784 amino acids (SEQ ID NO: 2) as given in the specification, or its fragment having at least 300 contiguous amino acids and kinase activity; or (d) the complement of (a), (b), (c), or (d). INDEPENDENT CLAIMS are also included for: (1) an expression construct comprising a recombinant nucleic acid molecule comprising the nucleic acid molecule (I); (2) a host cell comprising a recombinant nucleic acid molecule comprising the nucleic acid molecule (I); (3) an isolated polypeptide comprising: (a) a polypeptide which is encoded by a nucleic acid molecule comprising a nucleotide sequence with SEQ ID NO: 1 or 3; (b) a fragment of a polypeptide comprising the amino acid sequence of SEQ ID NO:2, where the fragment comprises at least 300 contiguous amino acids of SEQ ID NO:2 and where at least 300 contiguous amino acids have kinase activity; (c) an antigenic fragment of SEQ ID NO:2 comprising at least 15 amino acid residues of SEQ ID NO:2; or (d) a polypeptide having the amino acid sequence of SEQ ID NO:2; (4) an antibody which selectively binds to a polypeptide of (3); (5) producing a polypeptide of (3), comprising culturing the host cell of (2) under conditions in which the nucleic acid molecule is expressed; (6) a kit comprising a compound which selectively binds to a polypeptide of (3) and instructions for use; (7) a kit comprising a compound which selectively hybridizes to a nucleic acid molecule (I) and instructions for use; (8) identifying a compound which binds to a polypeptide of (3), comprising contacting a polypeptide, or a cell expressing the polypeptide with a test compound and determining whether the polypeptide binds to the test compound; (9) modulating the activity of a polypeptide of (3), comprising contacting a polypeptide or a cell expressing the polypeptide with a compound which binds to the polypeptide in a sufficient concentration to modulate the activity of the polypeptide; (10) identifying a compound which modulates the activity of a polypeptide of (3), comprising contacting the polypeptide with a test compound and determining the effect of the test compound on the activity of the polypeptide to therefore identify a compound that modulates the activity of the polypeptide; (11) identifying a subject having a disorder or at risk of developing a disorder selected from the group consisting of cancer, an immunological disorder, a viral disorder and an apoptotic disorder, comprising contacting a sample obtained from the subject comprising nucleic acid molecules with a nucleic acid probe or primer which selectively hybridizes to the nucleic acid molecule (I), and detecting in the sample the presence of a nucleic acid molecule which hybridizes to the probe or primer, therefore identifying a subject having the disorder, or at risk for developing the disorder; or comprising contacting a sample obtained from the subject comprising polypeptides with a compound which selectively binds to the polypeptide of (3), and detecting in the sample the presence of a polypeptide which binds to the compound, therefore, identifying a subject having the disorder, or at risk for developing the disorder; and (12) treating a subject having a disorder selected from the group consisting of cancer, an immunological disorder, a viral disorder and an apoptotic disorder comprising administering to the subject an effective amount of an agent which targets the expression or activity of a nucleic acid molecule (I).

BIOTECHNOLOGY - Preferred Nucleic Acid: The nucleic acid further comprises nucleic acid sequences encoding a heterologous polypeptide. Preferred Polypeptide: The polypeptide of (3) further comprises

heterologous amino acid sequences. Preferred Antibody: The antibody preferably binds to an antigenic fragment of SEQ ID NO: 2 selected from the group consisting of a fully defined sequence of 21, 20 or 21 bp (base pairs) (SEQ ID NO: 17, 18 and 19), as given in the specification. Preferred Method: The binding of the test compound to the polypeptide in the method of (8) is detected by detection of binding by direct detecting of test compound/polypeptide binding, detection of binding using a competition binding assay, or detection of binding using an assay for protein kinase-mediated phosphorylation. The activity of the polypeptide in the method of (10) is determined in a kinase assay using a **14171 kinase** substrate. The nucleic acid probe or primer in the method of (11) is from a fully defined sequence of 20, 20 or 26 bp (SEQ ID NO: 9, 10 or 11) as given in the specification.

ACTIVITY - Cytostatic; Virucide; Antiinflammatory; Cardiant; Antiarrhythmic; Hypotensive. No biological data given.

MECHANISM OF ACTION - Protein-Kinase-Modulator. No biological data given.

USE - The methods and compositions of the present invention are useful for the diagnosis and/or treatment of diseases or conditions associated with aberrant expression or activity of a 14171 protein kinase, such as cancer, an immunological disorder, inflammation, heart failure, hypertension, atrial fibrillation, a viral disorder and an apoptotic disorder. They can also be used in chromosome mapping, tissue typing, predictive medicine, forensic biology and prognostic assays.

ADMINISTRATION - Dosage of the pharmaceutical composition ranges from 0.001-30 mg/kg body weight, preferably 5-6 mg/kg. Routes of administration of the pharmaceutical compositions include oral, pulmonary, intramuscular, intraperitoneal, intravenous, subcutaneous, inhalation, transdermal, nasal and rectal.

EXAMPLE - Total RNA was prepared from various human tissues by a single step extraction method using RNA STAT-60. Each RNA preparation was treated with DNase I at 37 degrees centigrade for 1 hour. DNase I treatment was determined to be complete if the sample required at least 38 PCR amplification cycles to reach a threshold level of fluorescence using beta-2 microglobulin as an internal amplicon reference. After phenol extraction cDNA was prepared from the sample using SUPERSCRIPT Choice System. A negative control of RNA without reverse transcriptase was mock reverse transcribed for each RNA sample. (62 pages)

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=> d his

     (FILE 'HOME' ENTERED AT 12:20:43 ON 07 APR 2006)

     FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS,
     LIFESCI' ENTERED AT 12:21:52 ON 07 APR 2006
L1             1 S "14171 KINASE?"

=> s kinase?
L2       1434878 KINASE?

=> s clon? or express? or recombinant
L3       7629584 CLON? OR EXPRESS? OR RECOMBINANT

=> s "T-P" motif
L4            73 "T-P" MOTIF

=> s l2 and l4
L5            49 L2 AND L4

=> dup rem l5
PROCESSING COMPLETED FOR L5
L6            12 DUP REM L5 (37 DUPLICATES REMOVED)
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=> d 1-12 ibib ab

L6 ANSWER 1 OF 12 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 2006100693 IN-PROCESS
DOCUMENT NUMBER: PubMed ID: 16365045
TITLE: The low density lipoprotein receptor-related protein 6 interacts with glycogen synthase **kinase** 3 and attenuates activity.
AUTHOR: Mi Kaihong; Dolan Philip J; Johnson Gail V W
CORPORATE SOURCE: Department of Psychiatry, University of Alabama at Birmingham, Birmingham, Alabama 35294-0017, USA.
CONTRACT NUMBER: NS051279 (NINDS)
SOURCE: The Journal of biological chemistry, (2006 Feb 24) Vol. 281, No. 8, pp. 4787-94. Electronic Publication: 2005-12-19.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: NONMEDLINE; IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE: Entered STN: 20060222
Last Updated on STN: 20060314

AB Glycogen synthase **kinase** 3 (GSK3) is a widely expressed Ser/Thr protein **kinase** that phosphorylates numerous substrates. This large number of substrates requires precise and specific regulation of GSK3 activity, which is achieved by a combination of phosphorylation, localization, and interactions with GSK3-binding proteins. Members of the Wnt canonical pathway have been shown to influence GSK3 activity. Through a yeast two-hybrid screen, we identified the Wnt canonical pathway co-receptor protein low density lipoprotein receptor-related protein 6 (LRP6) as a GSK3-binding protein. The interaction between the C terminus of LRP6 and GSK3 was also confirmed by in vitro GST pull-down assays and in situ coimmunoprecipitation assays. In vitro assays using immunoprecipitated proteins demonstrated that the C terminus of LRP6 significantly attenuated the activity of GSK3beta. In situ, LRP6 significantly decreased GSK3beta-mediated phosphorylation of tau at both primed and unprimed sites. Finally, it was also demonstrated that GSK3beta phosphorylates the PPP(S/T)P **motifs** in the C terminus of LRP6. This is the first identification of a direct interaction between LRP6 and GSK3, which results in an attenuation of GSK3 activity.

L6 ANSWER 2 OF 12 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2004100692 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14681225
TITLE: Extracellular signal-regulated **kinases** 1/2 are serum-stimulated "Bim(EL) **kinases**" that bind to the BH3-only protein Bim(EL) causing its phosphorylation and turnover.
AUTHOR: Ley Rebecca; Ewings Katherine E; Hadfield Kathryn; Howes Elizabeth; Balmanno Kathryn; Cook Simon J
CORPORATE SOURCE: Laboratory of Molecular Signalling, Signalling Programme, The Babraham Institute, Cambridge CB2 4AT, United Kingdom.. becky.ley@bbsrc.ac.uk
SOURCE: The Journal of biological chemistry, (2004 Mar 5) Vol. 279, No. 10, pp. 8837-47. Electronic Publication: 2003-12-17.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200407
ENTRY DATE: Entered STN: 20040302
Last Updated on STN: 20040707

Entered Medline: 20040706

AB Bim, a "BH3-only" protein, is expressed de novo following withdrawal of serum survival factors and promotes cell death. We have shown previously that activation of the ERK1/2 pathway promotes phosphorylation of Bim(EL), targeting it for degradation via the proteasome. However, the nature of the **kinase** responsible for Bim(EL) phosphorylation remained unclear. We now show that Bim(EL) is phosphorylated on at least three sites in response to activation of the ERK1/2 pathway. By using the peptidylprolyl isomerase, Pin1, as a probe for proline-directed phosphorylation, we show that ERK1/2-dependent phosphorylation of Bim(EL) occurs at **(S/T)P motifs**. ERK1/2 phosphorylates Bim(EL), but not Bim(S) or Bim(L), in vitro, and mutation of Ser(65) to alanine blocks the phosphorylation of Bim(EL) by ERK1/2 in vitro and in vivo and prevents the degradation of the protein following activation of the ERK1/2 pathway. We also find that ERK1/2, but not JNK, can physically associate with GST-Bim(EL), but not GST-Bim(L) or GST-Bim(S), in vitro. ERK1/2 also binds to full-length Bim(EL) in vivo, and we have localized a potential ERK1/2 "docking domain" lying within a 27-amino acid stretch of the Bim(EL) protein. Our findings provide new insights into the post-translational regulation of Bim(EL) and the role of the ERK1/2 pathway in cell survival signaling.

L6 ANSWER 3 OF 12 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
DUPLICATE 3

ACCESSION NUMBER: 2005:89678 BIOSIS
DOCUMENT NUMBER: PREV200500087142
TITLE: Physiological role of the oxidative stress-susceptible TRPM2 Ca2+ channel in immunocytes.
AUTHOR(S): Yamamoto, Shinichiro [Reprint Author]; Shimizu, Shunichi; Ishii, Masakazu; Hagiwara, Tamio; Hara, Yuji; Negoro, Takaharu; Nishida, Motohiro; Tobe, Takashi; Mori, Yasuo; Kiuchi, Yuji
CORPORATE SOURCE: Grad Sch EngnDept Synthet Chem and BiolMol Biol Lab, Kyoto Univ, Kyoto, 6068501, Japan
SOURCE: Yakugaku Zasshi, (2004) Vol. 124, No. Suppl. 4, pp. 237-240. print.
ISSN: 0031-6903 (ISSN print).
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 2 Mar 2005
Last Updated on STN: 2 Mar 2005

AB TRPM2 is a Ca2+ permeable channel activated by various triggers including the oxidative stress including hydrogen peroxide (H2O2). TRPM2 is expressed in immunocytes such as monocytes, lymphocytes, and neutrophils. However its physiological role is unclear. Although the activation of TRPM2 by H2O2 seems to be mediated by NAD+ and/or ADP-ribose, the activation mechanisms in the context of physiological signaling are not elucidated. Thus, We investigated the activation mechanisms of TRPM2 and the physiological role of Ca2+ influx via TRPM2 using monocytic cell line U937. Addition of H2O2 to U937 cells triggered Ca2+ influx, and the both Ca2+ influx and TRPM2 expression were attenuated by the treatment with TRPM2-specific siRNA. The H2O2-triggered TRPM2 activation was also inhibited by the treatment with ERK **kinase** inhibitor, PD98059. Moreover, the activation of TRPM2 recombinantly expressed in HEK293 cells was blocked by the mutation of putative phosphorylation sites (**S/T -P motif**) by ERK, suggesting that H2O2-triggered TRPM2 activation was controlled by ERK pathway. In U937 cells, H2O2 induced interleukin-8 (IL-8) production in extracellular Ca2+ dependent manner, which was inhibited by the treatment with TRPM2 specific siRNA and PD98059. The Ca2+ influx via TRPM2 induced by H2O2 participates in IL-8 production in U937 cells.

L6 ANSWER 4 OF 12 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2004000668 EMBASE
TITLE: [Unexpected roles of the peptidyl-prolyl cis/trans isomerase Pin1].
PIN1: UNE PEPTIDYL-PROLYL CIS/TRANS ISOMERASE AUX ROLES INSOUPCONNES.
AUTHOR: Lavoie S.B.; Albert A.L.; Vincent M.
CORPORATE SOURCE: S.B. Lavoie, Departement de Medecine et CREFSIP, Pavillon C.E. Marchand, Universite Laval, Quebec, Que. G1K 7P4, Canada. seb_lavoie@iquebec.com
SOURCE: Medecine/Sciences, (2003) Vol. 19, No. 12, pp. 1251-1258. . Refs: 40
ISSN: 0767-0974 CODEN: MSMSE4
COUNTRY: France
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
008 Neurology and Neurosurgery
029 Clinical Biochemistry
LANGUAGE: French
SUMMARY LANGUAGE: English; French
ENTRY DATE: Entered STN: 16 Jan 2004
Last Updated on STN: 16 Jan 2004

AB Peptidyl-prolyl isomerases (PPlases) are chaperone enzymes which alter the peptide bond between a given amino acid and a proline, changing it from the as to the trans conformation and vice versa. This modification can cause dramatic structural modifications which can affect the properties of targeted proteins. The ubiquitous PPlase Pin1, conserved from yeast to human, has been shown to be necessary for entry into mitosis. The yeast homologue, Ess1, is essential for cell survival. Pin1 possesses a WW domain which specificaly recognizes pSer-Pro and pThr-Pro motifs in which the first amino acid is phosphorylated. Pin1 binds to many proteins implicated in cell cycle regulation (e.g. p53, Myt1, Wee1, and Cdc25C). Pin1 also targets tau, a protein forming part of the neuronal cytoskeleton which is hyperphosphorylated in patients suffering from Alzheimer's disease (AD). Pin1 could, therefore, be involved in the pathogenesis of AD. Furthermore, Pin1 also binds two proteins involved in transcription: Rpb1, the largest subunit of RNA polymerase 11 and Spt5, a regulator of the elongation of transcription. Both these proteins possess domains rich in S/T-P **motifs** which can be targeted by Pin1 when phosphorylated. Recent studies show that Pin1 modulates the dephosphorylation of some proteins by allowing trans-specific phosphatases to recognize their target after isomerization. This unexpected role might allow protein regulation via peptidyl-prolyl isomerase activity.

L6 ANSWER 5 OF 12 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 2001:245224 BIOSIS
DOCUMENT NUMBER: PREV200100245224
TITLE: IRS-1-dependent IFNalpha signaling is impaired by a FRAP regulated mechanism.
AUTHOR(S): Hartman, Matthew E. [Reprint author]; Villela-Bach, Montserrat [Reprint author]; Chen, Jie; Freund, Gregory G. [Reprint author]
CORPORATE SOURCE: University of Illinois at Urbana-Champaign, 1201 West Gregory, 261 ERML, Urbana, IL, 61801, USA
SOURCE: FASEB Journal, (March 8, 2001) Vol. 15, No. 5, pp. A945. print.
Meeting Info.: Annual Meeting of the Federation of American Societies for Experimental Biology on Experimental Biology 2001. Orlando, Florida, USA. March 31-April 04, 2001.
CODEN: FAJOEC. ISSN: 0892-6638.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 23 May 2001
Last Updated on STN: 19 Feb 2002

AB We have previously shown that interferon-alpha (IFNalpha)-dependent tyrosine phosphorylation of insulin receptor substrate-1 (IRS-1) and subsequent IRS-1 phosphatidylinositol 3-**kinase** (PI 3-**kinase**) association/activation is impaired by serine phosphorylation of IRS-1 due to the reduced ability of serine phosphorylated IRS-1 to serve as a substrate for Janus **kinase** 1 (JAK1). Here we report that FKBP12-rapamycin associated protein (FRAP) is a physiologic IRS-1 serine **kinase** that blocks IFNalpha signaling by serine phosphorylating IRS-1. We found that treatment of U266 cells with the FRAP inhibitor rapamycin increased IFNalpha-dependent tyrosine phosphorylation by 2-fold while reducing constitutive IRS-1 serine phosphorylation within S/**T-P motifs** by 80%. On the contrary, wortmannin treatment had no effect on IFNalpha stimulated IRS-1 tyrosine phosphorylation. Importantly, both FRAP and insulin-activated p70s6k, serine phosphorylated IRS-1 between residues 511-772 (IRS-1511-772), but only FRAP-dependent IRS-1511-772 serine phosphorylation inhibited by 50% subsequent JAK1-dependent tyrosine phosphorylation of IRS-1. Taken together, these data indicate that FRAP, but not p70s6k, is an in vivo IRS-1 serine **kinase** that negatively regulates JAK1-dependent IRS-1 tyrosine phosphorylation and suggest that FRAP may modulate cytokine signal transduction through IRSs.

L6 ANSWER 6 OF 12 MEDLINE on STN DUPLICATE 4
ACCESSION NUMBER: 2001179452 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11162588
TITLE: Frap-dependent serine phosphorylation of IRS-1 inhibits IRS-1 tyrosine phosphorylation.
AUTHOR: Hartman M E; Villela-Bach M; Chen J; Freund G G
CORPORATE SOURCE: Department of Animal Sciences, University of Illinois at Urbana-Champaign, Urbana, Illinois 61801, USA.
CONTRACT NUMBER: CA-61931 (NCI)
GM-58064 (NIGMS)
SOURCE: Biochemical and biophysical research communications, (2001 Jan 26) Vol. 280, No. 3, pp. 776-81.
Journal code: 0372516. ISSN: 0006-291X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200103
ENTRY DATE: Entered STN: 20010404
Last Updated on STN: 20010404
Entered Medline: 20010329

AB We have previously shown that interferon-alpha (IFN alpha)-dependent tyrosine phosphorylation of insulin receptor substrate-1 (IRS-1) is impaired by serine phosphorylation of IRS-1 due to the reduced ability of serine phosphorylated IRS-1 to serve as a substrate for Janus **kinase** 1 (JAK1). Here we report that FKBP12-rapamycin-associated protein (FRAP) is a physiologic IRS-1 **kinase** that blocks IFN alpha signaling by serine phosphorylating IRS-1. We found that both FRAP and insulin-activated p70 S6 **kinase** (p70(s6k)) serine phosphorylated IRS-1 between residues 511 and 772 (IRS-1(511-772)). Importantly, only FRAP-dependent IRS-1(511-772) serine phosphorylation inhibited by 50% subsequent JAK1-dependent tyrosine phosphorylation of IRS-1. Furthermore, treatment of U266 cells with the FRAP inhibitor rapamycin increased IFN alpha-dependent tyrosine phosphorylation by twofold while reducing constitutive IRS-1 serine phosphorylation within S/**T-P motifs** by 80%. Taken together, these data indicate that FRAP, but not p70(s6k), is a likely physiologic IRS-1 serine **kinase** that negatively regulates JAK1-dependent IRS-1 tyrosine phosphorylation and suggests that FRAP may modulate IRS-dependent cytokine signaling.

L6 ANSWER 7 OF 12 MEDLINE on STN DUPLICATE 5
ACCESSION NUMBER: 2000105769 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10637505
TITLE: ERK activation induces phosphorylation of Elk-1 at multiple S/T-P **motifs** to high stoichiometry.
AUTHOR: Cruzalegui F H; Cano E; Treisman R
CORPORATE SOURCE: Transcription Laboratory, Imperial Cancer Research Fund, 44 Lincoln's Inn Fields, London WC2A 3PX, UK.
SOURCE: Oncogene, (1999 Dec 23) Vol. 18, No. 56, pp. 7948-57. Journal code: 8711562. ISSN: 0950-9232.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200002
ENTRY DATE: Entered STN: 20000218
Last Updated on STN: 20000218
Entered Medline: 20000204

AB Elk-1, a member of the TCF family of Ets domain proteins, contains a C-terminal transcriptional activation domain with multiple copies of the MAPK core consensus sequence S/T-P. This region is phosphorylated by MAP **kinases** in vitro and in vivo, but the extent and kinetics of phosphorylation at the different sites have not been investigated in detail. We prepared antisera against the phosphorylated forms of residues T353, T363, T368, S383, S389 and T417. The antisera specifically recognize the phosphorylated Elk-1 C terminus and are specific for their cognate sites, as assessed by peptide competition and mutagenesis experiments. Analysis of cells stably expressing Elk-1 in vivo shows that following serum or TPA stimulation, residues T353, T363, T368, S383, S389 and T417 become phosphorylated with similar kinetics. Mutation of any one site does not prevent phosphorylation of the others. Mutation to alanine of S383, F378 or W379, which virtually abolishes transcriptional activation by Elk-1, does not affect phosphorylation of any sites tested. Analysis of Elk-1 using two-dimensional gel electrophoresis shows that following ERK activation Elk-1 receives at least six phosphates in addition to those present prior to stimulation. We propose that the Elk-1 C-terminal regulatory domain becomes stoichiometrically phosphorylated following growth factor stimulation.

L6 ANSWER 8 OF 12 MEDLINE on STN DUPLICATE 6
ACCESSION NUMBER: 1999009106 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9792705
TITLE: Mitogen-activated protein **kinase** phosphorylates and regulates the HIV-1 Vif protein.
AUTHOR: Yang X; Gabuzda D
CORPORATE SOURCE: Department of Cancer Immunology & AIDS, Dana-Farber Cancer Institute, Boston, Massachusetts 02115, USA.
CONTRACT NUMBER: AI28691 (NIAID)
AI36186 (NIAID)
AO6514
+
SOURCE: The Journal of biological chemistry, (1998 Nov 6) Vol. 273, No. 45, pp. 29879-87. Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; AIDS
ENTRY MONTH: 199812
ENTRY DATE: Entered STN: 19990115
Last Updated on STN: 19990115
Entered Medline: 19981210

AB The human immunodeficiency virus type 1 (HIV-1) Vif protein plays a

critical role in virus replication and infectivity. Here we show that Vif is phosphorylated and regulated by p44/42 mitogen-activated protein **kinase** (MAPK). Vif phosphorylation by MAPK was demonstrated in vitro as well as in vivo and was shown to occur on serine and threonine residues. Two-dimensional tryptic phosphopeptide mapping indicated that Vif is phosphorylated by MAPK on the same sites in vitro and in vivo. Radioactive peptide sequencing identified two phosphorylation sites, Thr96 and Ser165. These phosphorylation sites do not correspond to the known optimum consensus sequences for phosphorylation by MAPK (PX(S/T)P) nor to the minimum consensus sequence ((S/T)P), indicating that MAPK can phosphorylate proteins at sites other than those containing the PX(S/T)P or (S/T)P **motifs**. Synthetic Vif peptides corresponding to the local sequences of the phosphorylation sites were not phosphorylated by MAPK, suggesting that recognition of these sites by MAPK is likely to require structural determinants outside the phosphorylation site. Mutations of the Thr96 site, which is conserved among Vif sequences from HIV-1, HIV-2, and SIV, resulted in significant loss of Vif activity and inhibition of HIV-1 replication. These results suggest that MAPK plays a direct role in regulating HIV-1 replication and infectivity by phosphorylating Vif and identify a novel mechanism for activation of HIV-1 replication by mitogens and other extracellular stimuli.

L6 ANSWER 9 OF 12 MEDLINE on STN DUPLICATE 7
ACCESSION NUMBER: 1999030926 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9811754
TITLE: Host cell-virus cross talk: phosphorylation of a hepatitis B virus envelope protein mediates intracellular signaling.
AUTHOR: Rothmann K; Schnolzer M; Radziwill G; Hildt E; Moelling K; Schaller H
CORPORATE SOURCE: Zentrum fur Molekulare Biologie Heidelberg, D-69124 Heidelberg, Germany.
SOURCE: Journal of virology, (1998 Dec) Vol. 72, No. 12, pp. 10138-47.
Journal code: 0113724. ISSN: 0022-538X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199811
ENTRY DATE: Entered STN: 19990115
Last Updated on STN: 20000303
Entered Medline: 19981130

AB Phosphorylation of cytosolic pre-S domains of the duck hepatitis B virus (DHBV) large envelope protein (L) was identified as a regulatory modification involved in intracellular signaling. By using biochemical and mass spectrometric analyses of phosphopeptides obtained from metabolically radiolabeled L protein, a single phosphorylation site was identified at serine 118 as part of a PX(S/T)P **motif**, which is strongly preferred by ERK-type mitogen-activated protein **kinases** (MAP **kinases**). ERK2 specifically phosphorylated L at serine 118 in vitro, and L phosphorylation was inhibited by a coexpressed MAP **kinase**-specific phosphatase. Furthermore, L phosphorylation and ERK activation were shown to be induced in parallel by various stimuli. Functional analysis with transfected cells showed that DHBV L possesses the ability to activate gene expression in trans and, by using mutations eliminating (S-->A) or mimicking (S-->D) serine phosphorylation, that this function correlates with L phosphorylation. These mutations had, however, no major effects on virus production in cell culture and in vivo, indicating that L phosphorylation and transactivation are not essential for hepadnavirus replication and morphogenesis. Together, these data suggest a role of the L protein in intracellular host-virus cross talk by varying the levels of pre-S phosphorylation in response to the state of the cell.

L6 ANSWER 10 OF 12 MEDLINE on STN DUPLICATE 8
ACCESSION NUMBER: 1998256424 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9592139
TITLE: SCP2: a major protein component of the axial elements of synaptonemal complexes of the rat.
AUTHOR: Offenberg H H; Schalk J A; Meuwissen R L; van Aalderen M; Kester H A; Dietrich A J; Heyting C
CORPORATE SOURCE: Department of Genetics, Agricultural University, Dreijenlaan 2, NL-6703 HA Wageningen, The Netherlands.
SOURCE: Nucleic acids research, (1998 Jun 1) Vol. 26, No. 11, pp. 2572-9.
Journal code: 0411011. ISSN: 0305-1048.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-Y08981; GENBANK-Y08982
ENTRY MONTH: 199807
ENTRY DATE: Entered STN: 19980731
Last Updated on STN: 20000303
Entered Medline: 19980720

AB In the axial elements of synaptonemal complexes (SCs) of the rat, major protein components have been identified, with relative electrophoretic mobilities (M rs) of 30 000-33 000 and 190 000. Using monoclonal anti-SC antibodies, we isolated cDNA fragments which encode the 190 000 M r component of rat SCs. The translation product predicted from the nucleotide sequence of the cDNA, called SCP2 (for synaptonemal complex protein 2), is a basic protein (pI = 8.0) with a molecular mass of 173 kDa. At the C-terminus, a stretch of approximately 50 amino acid residues is predicted to be capable of forming coiled-coil structures. SCP2 contains two clusters of S/T-P motifs, which are common in DNA-binding proteins. These clusters flank the central, most basic part of the protein (pI = 9.5). Three of the S/T-P motifs are potential target sites for p34(cdc2) protein kinase. In addition, SCP2 has eight potential cAMP/cGMP-dependent protein kinase target sites. The gene encoding SCP2 is transcribed specifically in the testis, in meiotic prophase cells. At the amino acid sequence and secondary structural level, SCP2 shows some similarity to the Red1 protein, which is involved in meiotic recombination and the assembly of axial elements of SCs in yeast. We speculate that SCP2 is a DNA-binding protein involved in the structural organization of meiotic prophase chromosomes.

L6 ANSWER 11 OF 12 SCISEARCH COPYRIGHT (c) 2006 The Thomson Corporation on STN DUPLICATE 9
ACCESSION NUMBER: 1995:391391 SCISEARCH
THE GENUINE ARTICLE: RC664
TITLE: COMPARATIVE-ANALYSIS OF THE TERNARY COMPLEX FACTORS ELK-1, SAP-1A AND SAP-2 (ERP/NET)
AUTHOR: PRICE M A (Reprint); ROGERS A E; TREISMAN R
CORPORATE SOURCE: IMPERIAL CANC RES FUND, TRANSCRIPT LAB, 44 LINCOLNS INN FIELDS, LONDON WC2A 3PX, ENGLAND (Reprint)
COUNTRY OF AUTHOR: ENGLAND
SOURCE: EMBO JOURNAL, (1 JUN 1995) Vol. 14, No. 11, pp. 2589-2601.
ISSN: 0261-4189.
PUBLISHER: OXFORD UNIV PRESS UNITED KINGDOM, WALTON ST JOURNALS DEPT, OXFORD, ENGLAND OX2 6DP.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 45
ENTRY DATE: Entered STN: 1995
Last Updated on STN: 1995
*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS*

AB A transcription factor ternary complex composed of Serum Response Factor (SRF) and Ternary Complex Factor (TCF) mediates the response of the c-fos Serum Response Element (SRE) to growth factors and mitogens. Three Ets domain proteins, Elk-1, SAP-1 and ERP/NET, have been reported to have the properties of TCF. Here we compare Elk-1 and SAP-1a with the human ERP/NET homologue SAP-2. All three TCF RNAs are ubiquitously expressed at similar relative levels. All three proteins contain conserved regions that interact with SRF and the c-fos SRE with comparable efficiency, but in vitro complex formation by SAP-2 is strongly inhibited by its C-terminal sequences. Similarly, only Elk-1 and SAP-1a efficiently bind the c-fos SRE in vivo; ternary complex formation by SAP-2 is weak and is substantially unaffected by serum stimulation or v-ras co-expression. All three TCFs contain C-terminal transcriptional activation domains that are phosphorylated following growth factor stimulation. Activation requires conserved S/T-P **motifs** found in all the TCF family members, Each TCF activation domain can be phosphorylated in vitro by partially purifed ERK2, and ERK activation in vivo is sufficient to potentiate transcriptional activation.

L6 ANSWER 12 OF 12 MEDLINE on STN DUPLICATE 10
ACCESSION NUMBER: 92317057 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1618840
TITLE: Purification and characterization of a novel proline-directed protein **kinase** from bovine brain.
AUTHOR: Lew J; Beaudette K; Litwin C M; Wang J H
CORPORATE SOURCE: Department of Medical Biochemistry, Faculty of Medicine, University of Calgary, Alberta, Canada.
SOURCE: The Journal of biological chemistry, (1992 Jul 5) Vol. 267, No. 19, pp. 13383-90.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199208
ENTRY DATE: Entered STN: 19920815
Last Updated on STN: 19970203
Entered Medline: 19920805

AB A novel protein **kinase** which phosphorylates a synthetic peptide substrate (RRPDAHRTPNRAF) has been purified approximately 200,000-fold from bovine brain. This peptide contains the consensus sequence for phosphorylation by the p34cdc2 **kinase**. The purification procedure took advantage of the phenomenon that this novel brain **kinase**, in partially purified extracts, chromatographed on a gel filtration column as a high molecular weight complex which dissociated in buffer containing 1 M NaCl. The purified native enzyme was estimated to be approximately 63,000, and displayed two bands of M(r) = 33,000 and 25,000 on sodium dodecyl sulfate-polyacrylamide gel electrophoresis. On Western immunoblot, the M(r) = 33,000 peptide reacted strongly with antibodies specific for a conserved amino-terminal sequence, weakly with antibodies to the conserved PSTAIRE sequence, and not at all with antibodies to the carboxyl terminus, of HeLa cell p34cdc2. The brain **kinase** and p34cdc2 were similar in displaying good activity toward the parent peptide substrate, but no activity toward peptide analogues in which the -T-P- **motif** was substituted with either -T-G- or -T-A-. Both **kinases** showed marked preference in phosphorylating a peptide derived from H1 histone (KTPKKAKKPKTPKKAKKL), and both **kinases** could be phosphorylated by the src-family tyrosine **kinase**, p56lyn, purified from bovine spleen. However, the brain **kinase** did not co-purify with a subunit having a molecular weight corresponding to known cyclins, nor did it undergo specific interaction with p13suc1 beads, suggesting that this enzyme is distinct from p34cdc2.

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     FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS,
     LIFESCI' ENTERED AT 12:21:52 ON 07 APR 2006
L1             1 S "14171 KINASE?"
L2       1434878 S KINASE?
L3       7629584 S CLON? OR EXPRESS? OR RECOMBINANT
L4            73 S "T-P" MOTIF
L5            49 S L2 AND L4
L6            12 DUP REM L5 (37 DUPLICATES REMOVED)

=> s (modulat? or activat? or inhibit? ) and l2
L7       947418 (MODULAT? OR ACTIVAT? OR INHIBIT? ) AND L2

=> s "14171"
L8           42 "14171"

=> s l7 and l8
L9            2 L7 AND L8

=> d 1-2 ibib ab

L9    ANSWER 1 OF 2  BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
ACCESSION NUMBER: 2004-12766  BIOTECHDS
TITLE:            New 14171 protein kinase and nucleic
                  acid, useful for diagnosing or treating diseases with
                  aberrant expression of the 14171 protein
                  kinase, such as cancer, an immunological disorder,
                  inflammation, heart failure and hypertension;
                     recombinant enzyme protein production via plasmid
                     expression in host cell for use in disease therapy
AUTHOR:           KAPELLER-LIBERMANN R
PATENT ASSIGNEE:  MILLENNIUM PHARM INC
PATENT INFO:      US 2004048305 11 Mar 2004
APPLICATION INFO: US 2003-658904 10 Sep 2003
PRIORITY INFO:    US 2003-658904 10 Sep 2003; US 2000-182096 11 Feb 2000
DOCUMENT TYPE:    Patent
LANGUAGE:         English
OTHER SOURCE:     WPI: 2004-226195 [21]
AB    DERWENT ABSTRACT:
      NOVELTY - An isolated nucleic acid molecule (I) comprising a fully
      defined sequence of 3860 or 2355 base pairs (bp) (SEQ ID NO: 1 and 3) as
      given in the specification; a fragment of a fully defined sequence of 21
      bp (SEQ ID NO: 21, 22 or 23) as given in the specification; or encoding a
      polypeptide having a fully defined sequence of 784 amino acids (SEQ ID
      NO: 2) as given in the specification, is new.
           DETAILED DESCRIPTION - An isolated nucleic acid molecule comprises:
      (a) a fully defined sequence of 3860 or 2355 bp (SEQ ID NO: 1 and 3) as
      given in the specification; (b) a fragment of a fully defined sequence of
      21 bp (SEQ ID NO: 21, 22 or 23) as given in the specification; (c) a
      nucleic acid molecule which encodes a polypeptide having a fully defined
      sequence of 784 amino acids (SEQ ID NO: 2) as given in the specification,
      or its fragment having at least 300 contiguous amino acids and
      kinase activity; or (d) the complement of (a), (b), (c), or (d).
      INDEPENDENT CLAIMS are also included for: (1) an expression construct
      comprising a recombinant nucleic acid molecule comprising the nucleic
      acid molecule (I); (2) a host cell comprising a recombinant nucleic acid
      molecule comprising the nucleic acid molecule (I); (3) an isolated
      polypeptide comprising: (a) a polypeptide which is encoded by a nucleic
      acid molecule comprising a nucleotide sequence with SEQ ID NO: 1 or 3;
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(b) a fragment of a polypeptide comprising the amino acid sequence of SEQ ID NO:2, where the fragment comprises at least 300 contiguous amino acids of SEQ ID NO:2 and where at least 300 contiguous amino acids have **kinase** activity; (c) an antigenic fragment of SEQ ID NO:2 comprising at least 15 amino acid residues of SEQ ID NO:2; or (d) a polypeptide having the amino acid sequence of SEQ ID NO:2; (4) an antibody which selectively binds to a polypeptide of (3); (5) producing a polypeptide of (3), comprising culturing the host cell of (2) under conditions in which the nucleic acid molecule is expressed; (6) a kit comprising a compound which selectively binds to a polypeptide of (3) and instructions for use; (7) a kit comprising a compound which selectively hybridizes to a nucleic acid molecule (I) and instructions for use; (8) identifying a compound which binds to a polypeptide of (3), comprising contacting a polypeptide, or a cell expressing the polypeptide with a test compound and determining whether the polypeptide binds to the test compound; (9) **modulating** the activity of a polypeptide of (3), comprising contacting a polypeptide or a cell expressing the polypeptide with a compound which binds to the polypeptide in a sufficient concentration to **modulate** the activity of the polypeptide; (10) identifying a compound which **modulates** the activity of a polypeptide of (3), comprising contacting the polypeptide with a test compound and determining the effect of the test compound on the activity of the polypeptide to therefore identify a compound that **modulates** the activity of the polypeptide; (11) identifying a subject having a disorder or at risk of developing a disorder selected from the group consisting of cancer, an immunological disorder, a viral disorder and an apoptotic disorder, comprising contacting a sample obtained from the subject comprising nucleic acid molecules with a nucleic acid probe or primer which selectively hybridizes to the nucleic acid molecule (I), and detecting in the sample the presence of a nucleic acid molecule which hybridizes to the probe or primer, therefore identifying a subject having the disorder, or at risk for developing the disorder; or comprising contacting a sample obtained from the subject comprising polypeptides with a compound which selectively binds to the polypeptide of (3), and detecting in the sample the presence of a polypeptide which binds to the compound, therefore, identifying a subject having the disorder, or at risk for developing the disorder; and (12) treating a subject having a disorder selected from the group consisting of cancer, an immunological disorder, a viral disorder and an apoptotic disorder comprising administering to the subject an effective amount of an agent which targets the expression or activity of a nucleic acid molecule (I).

BIOTECHNOLOGY - Preferred Nucleic Acid: The nucleic acid further comprises nucleic acid sequences encoding a heterologous polypeptide. Preferred Polypeptide: The polypeptide of (3) further comprises heterologous amino acid sequences. Preferred Antibody: The antibody preferably binds to an antigenic fragment of SEQ ID NO: 2 selected from the group consisting of a fully defined sequence of 21, 20 or 21 bp (base pairs) (SEQ ID NO: 17, 18 and 19), as given in the specification. Preferred Method: The binding of the test compound to the polypeptide in the method of (8) is detected by detection of binding by direct detecting of test compound/polypeptide binding, detection of binding using a competition binding assay, or detection of binding using an assay for protein **kinase**-mediated phosphorylation. The activity of the polypeptide in the method of (10) is determined in a **kinase** assay using a **14171 kinase** substrate. The nucleic acid probe or primer in the method of (11) is from a fully defined sequence of 20, 20 or 26 bp (SEQ ID NO: 9, 10 or 11) as given in the specification.

ACTIVITY - Cytostatic; Virucide; Antiinflammatory; Cardiant; Antiarrhythmic; Hypotensive. No biological data given.

MECHANISM OF ACTION - Protein-**Kinase**-**Modulator**. No biological data given.

USE - The methods and compositions of the present invention are

useful for the diagnosis and/or treatment of diseases or conditions associated with aberrant expression or activity of a **14171** protein **kinase**, such as cancer, an immunological disorder, inflammation, heart failure, hypertension, atrial fibrillation, a viral disorder and an apoptotic disorder. They can also be used in chromosome mapping, tissue typing, predictive medicine, forensic biology and prognostic assays.

ADMINISTRATION - Dosage of the pharmaceutical composition ranges from 0.001-30 mg/kg body weight, preferably 5-6 mg/kg. Routes of administration of the pharmaceutical compositions include oral, pulmonary, intramuscular, intraperitoneal, intravenous, subcutaneous, inhalation, transdermal, nasal and rectal.

EXAMPLE - Total RNA was prepared from various human tissues by a single step extraction method using RNA STAT-60. Each RNA preparation was treated with DNase I at 37 degrees centigrade for 1 hour. DNase I treatment was determined to be complete if the sample required at least 38 PCR amplification cycles to reach a threshold level of fluorescence using beta-2 microglobulin as an internal amplicon reference. After phenol extraction cDNA was prepared from the sample using SUPERSCRIPT Choice System. A negative control of RNA without reverse transcriptase was mock reverse transcribed for each RNA sample. (62 pages)

L9 ANSWER 2 OF 2 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
ACCESSION NUMBER: 2003-28808 BIOTECHDS
TITLE: New **14171** human protein **kinase** and nucleic acids encoding the protein, useful for treating viral infections, cellular growth related disorders, cancers, disorders related with programmed cell death, or autoimmune disorders;
vector-mediated protein-**kinase** gene transfer and expression in host cell for recombinant protein production, drug screening and gene therapy
AUTHOR: KAPELLER-LIBERMANN R
PATENT ASSIGNEE: MILLENNIUM PHARM INC
PATENT INFO: US 6630335 7 Oct 2003
APPLICATION INFO: US 2001-781882 12 Feb 2001
PRIORITY INFO: US 2001-781882 12 Feb 2001; US 2000-182096 11 Feb 2000
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2003-810551 [76]
AB DERWENT ABSTRACT:

NOVELTY - An isolated nucleic acid molecule (I) comprising: (a) a sequence of 3860 or 2355 bp given in the specification, or its complement; or (b) a sequence which encodes a polypeptide comprising a sequence of 784 amino acids (II) or the sequence (II) having a substitution for aspartate at position 143, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for: (1) a vector comprising (I); (2) a host cell comprising the vector; and (3) a method of producing a polypeptide comprising culturing the host cell of (2) under conditions in which the nucleic acid molecule is expressed to produce the polypeptide.

WIDER DISCLOSURE - (1) antibodies that selectively bind protein **kinase** polypeptide and fragments; (2) a method for detecting protein **kinase** activity of expression in a biological sample; (3) a method for **modulating** protein **kinase** activity; (4) a diagnostic assay for identifying the presence or absence of a genetic lesion for mutation characterized by aberrant modification or mutation of a gene encoding a protein **kinase**, misregulation of a gene encoding a protein **kinase**, or aberrant post-translational modification of a protein **kinase**; (5) a method for identifying a compound that binds to or **modulates** protein **kinase** activity; (6) a method for identifying compound that **modulates** the expression of a protein **kinase** gene; and (7) compound identified by the screening methods.

BIOTECHNOLOGY - Preferred Nucleic Acid: (I) further comprises nucleic acid sequences encoding a heterologous polypeptide. (I) comprises a sequence encoding a polypeptide comprising (II). Preferred Vector: The vector of comprises a nucleic acid sequence, which regulates expression of the nucleic acid molecule. Preferred Host Cell: The host cell is preferably a mammalian host cell.

ACTIVITY - Virucide; Hepatotropic; Cardiant; Hypotensive; Antianginal; Cytostatic; Neuroprotective; Nootropic; Antiparkinsonian; Anticonvulsant; Immunosuppressive; Antiinflammatory; Dermatological. Preferred Vector: The vector of comprises a nucleic acid sequence, which regulates expression of the nucleic acid molecule.

MECHANISM OF ACTION - Protein **Kinase**; Gene Therapy.

USE - The protein **kinase** or the nucleic acid encoding the protein is useful for **modulating** cellular growth, differentiation and/or development, and for **modulating** cellular metabolic pathways, particularly for regulating one or more proteins involved in growth and metabolism. (I) is also useful as primers or hybridization probes for detecting protein **kinase**-encoding nucleic acids, in tissue typing, chromosome mapping or forensic biology. These are also useful for treating viral infections (e.g. hepatitis B), cellular growth related disorders (e.g. heart failure, hypertension, atrial fibrillation, dilated and idiopathic cardiomyopathy or angina), proliferative or differentiative disorders such as cancer (e.g. liver, melanoma, prostate, cervical, breast, colon or sarcoma), disorders related with programmed cell death (e.g. Alzheimer's disease, Parkinson's disease or epilepsy), or autoimmune disorders (e.g. systemic lupus erythematosus).

ADMINISTRATION - Dosage is 0.001-30 mg/kg, preferably 1-10 mg/kg body weight. Administration can be through parenteral (e.g. intravenous, intradermal, subcutaneous), oral (e.g. inhalation), transdermal (topical), transmucosal or rectal routes.

EXAMPLE - No suitable example given.(50 pages)

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     FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS,
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L1             1 S "14171 KINASE?"
L2       1434878 S KINASE?
L3       7629584 S CLON? OR EXPRESS? OR RECOMBINANT
L4            73 S "T-P" MOTIF
L5            49 S L2 AND L4
L6            12 DUP REM L5 (37 DUPLICATES REMOVED)
L7        947418 S (MODULAT? OR ACTIVAT? OR INHIBIT? ) AND L2
L8            42 S "14171"
L9             2 S L7 AND L8

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E1             3     LIBERMANA/BI
E2            54     LIBERMANN/BI
E3             0 --> LIBERMANN ROSANNA/BI
E4             1     LIBERMANS/BI
E5             1     LIBERMEISTER/BI
E6             1     LIBERMORE/BI
E7             1     LIBERNAN/BI
E8             5     LIBERNETICAL/BI
E9             1     LIBERNIELLA/BI
E10          282     LIBERO/BI
E11           88     LIBEROBACTER/BI
E12            1     LIBEROBACTERIA/BI
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E1            1     LIBERMANIS OLAFS/AU
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E3            2 --> LIBERMANN/AU
E4            1     LIBERMANN A/AU
E5            1     LIBERMANN A D/AU
E6            1     LIBERMANN A M/AU
E7            1     LIBERMANN A N/AU
E8            2     LIBERMANN B/AU
E9            1     LIBERMANN B E/AU
E10           1     LIBERMANN B M/AU
E11           1     LIBERMANN BERND/AU
E12          23     LIBERMANN C/AU

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E2           36     KAPELLER PETER/AU
E3          103 --> KAPELLER R/AU
E4            4     KAPELLER REGINE/AU
E5            1     KAPELLER ROSAN/AU
E6           44     KAPELLER ROSANA/AU
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E8            2     KAPELLER RUDOLF/AU
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E10           3     KAPELLER SHE A M/AU
E11           1     KAPELLER W/AU
E12           1     KAPELLERADLER REGINE/AU

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L10         103 "KAPELLER R"/AU

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L2       1434878 S KINASE?
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L4            73 S "T-P" MOTIF
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L6            12 DUP REM L5 (37 DUPLICATES REMOVED)
L7        947418 S (MODULAT? OR ACTIVAT? OR INHIBIT? ) AND L2
L8            42 S "14171"
L9             2 S L7 AND L8
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                 E LIBERMANN/AU
                 E KAPELLER R/AU
L10          103 S E3

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L11            0 L8 AND L10

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L2       1434878 S KINASE?
L3       7629584 S CLON? OR EXPRESS? OR RECOMBINANT
L4            73 S "T-P" MOTIF
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L5            49 S L2 AND L4
L6            12 DUP REM L5 (37 DUPLICATES REMOVED)
L7        947418 S (MODULAT? OR ACTIVAT? OR INHIBIT? ) AND L2
L8            42 S "14171"
L9             2 S L7 AND L8
                 E LIBERMANN ROSANNA
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L10          103 S E3
L11            0 S L8 AND L10
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| | Issue Date | Pages | Document ID | Title |
|---|---|---|---|---|
| 1 | 20040311 | 62 | US 20040048305 A1 | 14171 Protein kinase, a novel human protein kinase and uses thereof |
| 2 | 20031007 | 50 | US 6630335 B1 | 14171 protein kinase, a novel human protein kinase and uses thereof |

| | Issue Date | Pages | Document ID | Title |
|---|---|---|---|---|
| 1 | 20060406 | 95 | US 20060075522 A1 | Genes and uses for plant improvement |
| 2 | 20060330 | 191 | US 20060068382 A1 | Isolated human transporter proteins, nucleic acid molecules encoding human transporter proteins, and uses thereof |
| 3 | 20060316 | 157 | US 20060057667 A1 | Isolated human transporter proteins nucleic acid molecules encoding human transporter proteins and uses thereof |
| 4 | 20060309 | 342 | US 20060051850 A1 | Isolated human transporter proteins, nucleic acid molecules encoding human transporter proteins, and uses thereof |
| 5 | 20060119 | 83 | US 20060014177 A1 | Stable protein storage and stable nucleic acid storage in recoverable form |
| 6 | 20051208 | 450 | US 20050271676 A1 | Inducing cellular immune responses to human immunodeficiency virus-1 using peptide and nucleic acid compositions |
| 7 | 20051103 | 540 | US 20050244834 A1 | Single nucleotide polymorphisms in genes |

| | | | | |
|---|---|---|---|---|
| 8 | 20051006 | 121 | US 20050221437 A1 | Isolated human transporter proteins, nucleic acid molecules encoding human transporter proteins, and uses thereof |

| | Issue Date | Pages | Document ID | Title |
|---|---|---|---|---|
| 9 | 20051006 | 397 | US 20050221311 A1 | Isolated human transporter proteins nucleic acid molecules encoding human transporter proteins and used thereof |
| 10 | 20050901 | 79 | US 20050191645 A1 | Isolated human transporter proteins, nucleic acid molecules encoding human transporter proteins, and uses thereof |
| 11 | 20050901 | 605 | US 20050191331 A1 | Medical implants and anti-scarring agents |
| 12 | 20050825 | 109 | US 20050186613 A1 | Isolated human transporter proteins, nucleic acid molecules encoding human transporter proteins, and uses thereof |
| 13 | 20050825 | 605 | US 20050183728 A1 | Medical implants and anti-scarring agents |
| 14 | 20050818 | 605 | US 20050181977 A1 | Medical implants and anti-scarring agents |
| 15 | 20050818 | 55 | US 20050181365 A1 | Isolated human transporter proteins, nucleic acid molecules encoding human transporter proteins, and uses thereof |
| 16 | 20050818 | 605 | US 20050181011 A1 | Medical implants and anti-scarring agents |
| 17 | 20050818 | 605 | US 20050181008 A1 | Medical implants and anti-scarring agents |

| | Issue Date | Pages | Document ID | Title |
|---|---|---|---|---|
| 18 | 20050811 | 603 | US 20050177225 A1 | Medical implants and anti-scarring agents |
| 19 | 20050811 | 605 | US 20050175663 A1 | Medical implants and anti-scarring agents |
| 20 | 20050804 | 151 | US 20050170413 A1 | Isolated human ion channel proteins, nucleic acid molecules encoding human ion channel proteins, and uses thereof |
| 21 | 20050728 | 605 | US 20050164858 A1 | Medical implants and anti-scarring agents |
| 22 | 20050728 | 45 | US 20050165219 A1 | Isolated human transporter proteins, nucleic acid molecules encoding human transporter proteins, and uses thereof |
| 23 | 20050728 | 38 | US 20050164291 A1 | Isolated human transporter proteins, nucleic acid molecules encoding human transporter proteins, and uses thereof |
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